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# UNIVERSITÀ DEGLI STUDI DI TORINO

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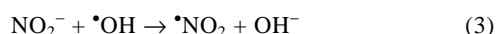
# THEORETICAL AND EXPERIMENTAL EVIDENCE OF THE PHOTONITRATION PATHWAY OF PHENOL AND 4-CHLOROPHENOL: A MECHANISTIC STUDY OF ENVIRONMENTAL SIGNIFICANCE

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Light-induced nitration pathways of phenols are important processes for the transformation of pesticide-derived secondary pollutants into toxic derivatives in surface waters, and for the formation of phytotoxic compounds in the atmosphere. Moreover, phenols can be used as  $\bullet\text{NO}_2$  probes in irradiated aqueous solutions. This paper shows that the nitration of 4-chlorophenol (4CP) into 2-nitro-4-chlorophenol (NCP) in the presence of irradiated nitrate and nitrite in aqueous solution involves the radical  $\bullet\text{NO}_2$ . The experimental data allow exclusion of an alternative nitration pathway by  $\bullet\text{OH} + \bullet\text{NO}_2$ . Quantum mechanical calculations suggest that the nitration of both phenol and 4CP involves as a first pathway the abstraction of the phenolic hydrogen by  $\bullet\text{NO}_2$ , which yields  $\text{HNO}_2$  and the corresponding phenoxy radical. It follows reaction of phenoxyl with another  $\bullet\text{NO}_2$  to finally produce the corresponding nitrated phenol. Such a pathway also correctly predicts that 4CP undergoes nitration more easily than phenol, because the ring Cl atom increases the acidity of the phenolic hydrogen of 4CP. This favours the H-abstraction process to give the corresponding phenoxy radical. In contrast, an alternative nitration pathway that involves  $\bullet\text{NO}_2$  addition to the ring followed by H-abstraction by oxygen (or by  $\bullet\text{NO}_2$  or  $\bullet\text{OH}$ ) is energetically unfavoured and erroneously predicts faster nitration for phenol than for 4CP.

## Introduction

The occurrence of aromatic nitroderivatives in the environment is a matter of concern because they have toxic effects.<sup>1</sup> Some of these compounds may also act as inhibitors of phenol sulfotransferase enzymes, which are involved into detoxification processes.<sup>2</sup> Moreover, nitroaromatic compounds can cause damage to DNA, which gives them potential for genotoxicity and mutagenicity.<sup>3,4</sup> Nitroaromatics can be directly emitted into the environment, but they are more often formed as secondary pollutants upon nitration of the corresponding aromatic precursors.<sup>5,6,7</sup> Nitration processes can take place in the gas phase,<sup>8,9</sup> on particles<sup>10</sup> and in surface and atmospheric waters.<sup>11,12,13</sup> In the aqueous solution and in particular in surface waters, a large fraction of nitroaromatic formation is thought to take place *via* photonitration reactions.<sup>14,15,16,17</sup> Such processes are induced by irradiation of nitrate and nitrite and involve at some level the photogeneration of  $\bullet\text{NO}_2$ . The formation of  $\bullet\text{NO}_2$  by photolysis of nitrate and nitrite takes place as follows:<sup>18</sup>



The described photochemical reactions can play a comparable role as the nitrogen dioxide dissolution from the gas phase, as  $\bullet\text{NO}_2$  sources in atmospheric waters.<sup>19</sup> In this compartment, the formation of phenolic nitroderivatives in the presence of

$\bullet\text{NO}_2$  is strongly suspected to substantially contribute to forest damage in polluted areas and in their downwind regions.<sup>20</sup>

Phenolic compounds are easily nitrated substrates and are the most studied chemicals as far as photonitration is concerned. It has for instance been shown that 4-chlorophenol (4CP), an environmental transformation intermediate of the herbicide dichlorprop, can undergo photonitration into 2-nitro-4-chlorophenol (NCP) in paddy-field water.<sup>16</sup> Nevertheless, the actual mechanism of phenol photonitration has been the object of debate.<sup>21,22</sup> Elucidation of this reaction pathway is very important for a better understanding of the environmental conditions that are most likely to favour the process. Moreover, the phenol photonitration reaction is a useful  $\bullet\text{NO}_2$  probe,<sup>14,16</sup> and the knowledge of the reaction mechanism is essential for a quantitative assessment of the  $\bullet\text{NO}_2$  occurrence in irradiated systems.

In the literature many computational studies are present that describe the mechanism of benzene or phenol nitration via  $\text{A}_{\text{ES}}$  operated by nitronium ion,<sup>23,24</sup> because of the relevance of this reaction for organic synthesis and industrial applications.<sup>25,26,27</sup> In contrast, little attention has been given to the nitration of phenolic compounds occurring via radical mechanisms,<sup>28,29</sup> because of the lower selectivity and of the difficulty to prepare large quantities of the reactant radical species. Because of the environmental interest of the photonitration processes, the present study is focused on the understanding of the nitration mechanism of phenolic compounds in irradiated systems, using both quantum calculations and experimental evidence.

## Experimental

### Reagents and materials

4-Chlorophenol (purity grade 99%), 2-nitro-4-chlorophenol (98%), anisole (99%), 2-nitroanisole (99%), 3-nitroanisole (98%) and 4-nitroanisole (97%) were purchased from Aldrich, acetonitrile (gradient grade), NaNO<sub>3</sub> (99%) and H<sub>3</sub>PO<sub>4</sub> (85%) from VWR Int., NaNO<sub>2</sub> (97%) from Carlo Erba. All reagents were used as received, without further purification.

### Irradiation experiments

Solution to be irradiated (5 mL) were placed in cylindrical Pyrex glass cells (4.0 cm diameter, 2.3 cm height) and irradiated under magnetic stirring with a Philips TL 01 UVB lamp, with maximum emission at 313 nm. The lamp irradiance was 9.5 W m<sup>-2</sup> (290-400 nm, measured with a power meter by CO.FO.ME.GRA., Milan, Italy) and the incident photon flux in solution was determined by ferrioxalate actinometry as  $P_o = \int_{\lambda} p^o(\lambda) d\lambda = 6.2 \cdot 10^{-6}$

Einstein L<sup>-1</sup> s<sup>-1</sup>. The lamp was chosen to achieve excitation of nitrate that absorbs radiation in the UVB region.<sup>18</sup>

After irradiation, the solutions were analysed by High Performance Liquid Chromatography (HPLC). The adopted Merck-Hitachi instrument was equipped with AS2000A autosampler (100 µL sample volume), L-6200 and L-6000 pumps for high-pressure gradients, Merck LiChrocart RP-C18 column packed with LiChrospher 100 RP-18 (125 mm × 4.6 mm × 5 µm), and L-4200 UV-Vis detector (detection wavelength was set at 220 nm). Isocratic elution was carried out with 40:60 CH<sub>3</sub>CN:aqueous H<sub>3</sub>PO<sub>4</sub> (pH 2.8) at 1.0 mL min<sup>-1</sup> flow rate. The retention times were (min): 4-chlorophenol (4CP, 4.2), 2-nitro-4-chlorophenol (NCP, 8.0), anisole (8.2), 2-nitroanisole (5.7), 3-nitroanisole (9.0), 4-nitroanisole (7.7). The column dead time was 0.9 min.

The time evolution curves of NCP were fitted with equations of the form  $C_{\text{NCP}}^{\text{NCP}} = k_{\text{NCP}}^f C_o (k_{\text{NCP}}^d - k_{4\text{CP}}^d)^{-1} [\exp(-k_{4\text{CP}}^d t) - \exp(-k_{\text{NCP}}^d t)]$ , where  $C_{\text{NCP}}^{\text{NCP}}$  is the concentration of NCP at the time  $t$ ,  $C_o$  the initial concentration of 4CP,  $k_{\text{NCP}}^f$  and  $k_{\text{NCP}}^d$  the pseudo-first order formation and transformation rate constants of NCP, respectively, and  $k_{4\text{CP}}^d$  the pseudo-first order transformation rate constant of 4CP. The initial formation rate of NCP is  $\text{Rate}_{\text{NCP}} = k_{\text{NCP}}^f C_o$ . The reproducibility of repeated runs was around 10-15%.

### Quantum mechanical calculations

A computational study of phenol and 4CP nitration mechanism was carried out using the density functional theory (DFT)<sup>30</sup>. DFT methods and in particular those using hybrid functionals have been widely employed to explore chemical reactions due to their good accuracy at a relatively low computational cost. They have been used for a large number of test molecules including radicals, non-hydrogen systems, aromatic and aliphatic hydrocarbons. In the present study, geometry optimisations of the ground state of all the involved species were carried out in the gas phase and were confirmed by analytical calculation of frequencies. For each molecular

species, the gas-phase optimised structures were determined by gradient procedures<sup>31</sup> within DFT with the B3LYP hybrid functional.<sup>32</sup> The latter is a well-performing functional for reactions involving radical species and aromatic compounds.<sup>33,34</sup> The polarised 6-311G(d,p) basis set was used in all the calculations. The nature of the stationary points, minima or saddle points, was confirmed by analytical calculation of the vibrational frequencies to evaluate the corresponding zero-point vibrational energies. Calculations were performed in the gas phase and were not refined with any solvation model.

The reason of this approximation is that radical-forming reactions are usually not very sensitive to medium effects, because activated complexes that produce neutral radicals normally exhibit no charge separation. As a consequence, they have a minor ability to interact with the solvent compared to charged species.<sup>35</sup> Furthermore, very limited stabilisation energy or geometry changes induced by the solvent are expected in the present case, in analogy with the results of calculations performed on similar systems where radical reactions were taking place.<sup>36,37,38</sup> Finally, the main goal of this work is the comparison of two reaction pathways *via* the ratio of their rate constants, derived from the respective energy barriers. The limited solvation effects that would take place are expected to influence both pathways at a similar extent. The resulting small energy changes would be largely compensated for when making the ratio of the rate constants.

All calculations were carried out with the GAUSSIAN 03W suite of programs.<sup>39</sup> The figures were generated with the GaussView program.

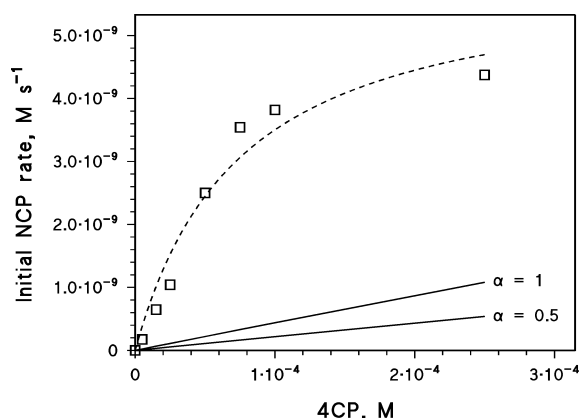
## Results and discussion

### Photonitration of phenolic compounds upon irradiation of nitrate and nitrite

In the case of phenol photonitration upon irradiation of nitrate and/or nitrite, there is wide evidence that the reaction involves •NO<sub>2</sub> and not •OH + •NO<sub>2</sub>.<sup>40</sup> A clear differentiation between the two possible pathways is to be provided for the photonitration of 4CP as well.

Figure 1 reports the initial formation rate of NCP as a function of the initial 4CP concentration, upon UVB irradiation of 0.10 M NaNO<sub>3</sub> + 0.01 M NaNO<sub>2</sub>. The NCP rate follows an initially linear trend but starts levelling off above 0.1 mM 4CP.

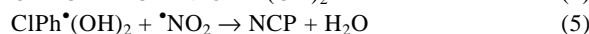
Upon application of the Lambert Beer's law to radiation absorption in mixtures under polychromatic irradiation (which involves procedures of numerical integration over wavelength),<sup>41</sup> one gets that the photon flux absorbed by 0.10 M nitrate in the system was  $P_a^{\text{NO}_3^-} = 1.8 \cdot 10^{-6}$  Einstein L<sup>-1</sup> s<sup>-1</sup>. For 0.01 M nitrite it was  $P_a^{\text{NO}_2^-} = 6.2 \cdot 10^{-7}$  Einstein L<sup>-1</sup> s<sup>-1</sup>.



**Figure 1.** Initial formation rate of NCP as a function of 4CP initial concentration, upon UVB irradiation of 0.10 M NaNO<sub>3</sub> + 0.01 M NaNO<sub>2</sub> at pH 6 in aerated solution. The solid lines represent the predicted rates by equation (8), with the reported  $\alpha$  values. The dashed curve is the fit of the experimental data with equation (13) (*vide infra*).

The quantum yields for  $\bullet$ OH formation by nitrate and nitrite under UVB irradiation are 0.01 and 0.065, respectively,<sup>18</sup> from which one gets the total  $\bullet$ OH formation rate in the system,  $R_{\bullet\text{OH}} = R_{\bullet\text{OH}}^{\text{NO}_3^-} + R_{\bullet\text{OH}}^{\text{NO}_2^-} = 0.01 P_a^{\text{NO}_3^-} + 0.065 P_a^{\text{NO}_2^-} = 5.8 \cdot 10^{-8} \text{ Einstein L}^{-1} \text{ s}^{-1}$ . The presence of  $\bullet$ OH scavengers at sufficiently elevated concentration (*e.g.* 1mM or higher) could increase the photolysis quantum yield of nitrate by affecting the early steps after the primary photolysis event,<sup>42,43</sup> but this is unlikely to take place at a significant extent with 4CP at the adopted sub-mM levels.

If the nitration of 4CP takes place via  $\bullet$ OH +  $\bullet$ NO<sub>2</sub>, a kinetic model applies that is made up of reactions (1-3) plus the following ones (where ClPhOH is 4CP and 4CP-OH is an hydroxyderivative of 4CP):



In alternative to O<sub>2</sub>, also  $\bullet$ OH and  $\bullet$ NO<sub>2</sub> could take part in reaction (6) as hydrogen-abstracting reagents. As an approximated approach to solve the kinetic system, the lumped reaction (7) incorporates various transformation processes for nitrogen dioxide, including the reaction with O<sub>2</sub> $\bullet$ .<sup>18</sup> Upon application of the steady-state approximation to  $\bullet$ NO<sub>2</sub>,  $\bullet$ OH and ClPh(OH)<sub>2</sub>, one gets the following result for the initial formation rate of NCP:

$$d[\text{NCP}]/dt = \alpha \cdot R_{\bullet\text{OH}} \cdot \frac{k_4[4\text{CP}]}{k_4[4\text{CP}] + k_3[\text{NO}_2^-]} \quad (8)$$

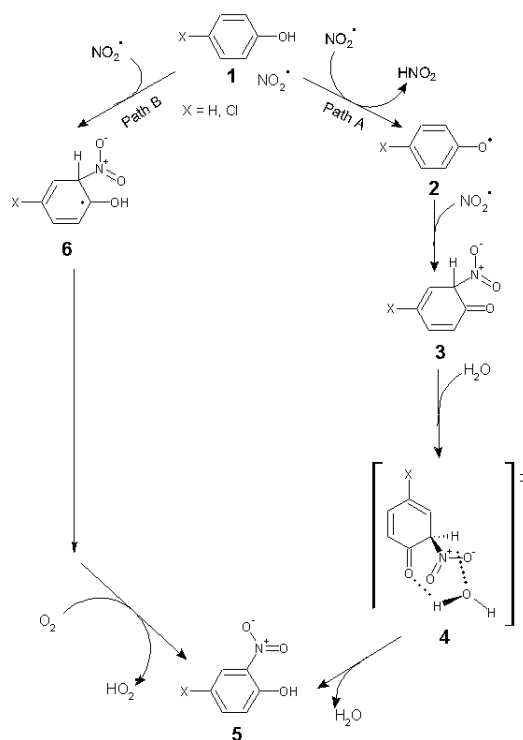
where  $k_4 = 7.6 \cdot 10^9 \text{ M}^{-1} \text{ s}^{-1}$  and  $k_3 = 1.0 \cdot 10^{10} \text{ M}^{-1} \text{ s}^{-1}$ .<sup>44</sup>  $\alpha = k_5 [\bullet\text{NO}_2] / (k_5 [\bullet\text{NO}_2] + k_6 [\text{O}_2])^{-1}$  is the fraction of the radical species ClPh(OH)<sub>2</sub> that reacts with  $\bullet$ NO<sub>2</sub> in reaction (5) to yield NCP, in competition with the reaction (6) with O<sub>2</sub> that produces the hydroxyderivative 4CP-OH. The NCP formation rates foreseen by equation (8) are reported as solid lines in

Figure 1, for  $\alpha = 1$  (reaction (5) much faster than (6)) and  $\alpha = 0.5$  (equal rates for the two reactions). The equation (8) rates are considerably lower than the experimental ones, and one should also consider that the assumptions  $\alpha = 1$  and  $\alpha = 0.5$  most likely represent an overestimate of the NCP rate via the proposed  $\bullet$ OH +  $\bullet$ NO<sub>2</sub> pathway. The formation rate of the hydroxyderivatives upon nitrate irradiation is in fact considerably higher than that of the nitroderivatives,<sup>45</sup> which suggests that reaction (5) would actually be much slower than (6). Therefore, the NCP formation rate via reactions (4-6) is expected to be even lower than is reported in Figure 1.

Figure 1 also shows that equation (8) foresees a linear trend with [4CP] of the NCP formation rate, in disagreement with the experimental data, because  $k_4[4\text{CP}] \ll k_3[\text{NO}_2^-]$ . The comparison between experimental data and model predictions clearly suggests that  $\bullet$ OH is involved at a minor to negligible extent in the nitration of 4CP. Therefore, the following discussion will only consider the possible pathways that may be involved in the nitration of phenol and of 4CP by  $\bullet$ NO<sub>2</sub>, excluding or neglecting the contribution of  $\bullet$ OH to the nitration process.

### Nitration pathways of phenolic compounds by $\bullet$ NO<sub>2</sub>

Two alternative mechanisms have been proposed for the photonitration of phenol by  $\bullet$ NO<sub>2</sub>,<sup>21,22</sup> which are reported in Scheme 1. We hypothesise the same processes for the photonitration of 4CP as well. Furthermore, because 4CP can only be nitrated in the *ortho* position with respect to the phenolic group, the *para* one being occupied by Cl, only the *ortho* nitration pathway is shown in Scheme 1.



**Scheme 1.** Reaction of nitrogen dioxide with phenol and 4CP via radical pathways.

The first mechanism (Path A) involves as primary step an hydrogen abstraction by  $\bullet\text{NO}_2$  from the phenolic OH group. In contrast, the second mechanism (Path B) foresees addition of nitrogen dioxide to the aromatic ring.

5 Path A starts with a H-transfer redox reaction that involves  $\bullet\text{NO}_2$  as the oxidant and phenol as the reductant. Such a process yields the phenoxyl radical **2** and nitrous acid. It follows addition of  $\bullet\text{NO}_2$  to **2** with production of **3**. In this pathway, the rearomatisation of **3** gives the 2-nitrophenol **5** through a hydrogen rearrangement catalysed by a water molecule. This step is likely to involve the transient **4**, as proposed by Houk for tyrosine nitration by peroxyxynitrite.<sup>46</sup>

In the alternative Path B, the addition of  $\bullet\text{NO}_2$  to the aromatic ring generates the intermediate **6**. The 2-nitrophenol **5** is formed from **6** by H abstraction, which restores the aromaticity of the ring. H abstraction can be carried out by dissolved  $\text{O}_2$  to produce the hydroperoxyl radical  $\text{HO}_2\bullet$ ; alternative reagents for the process are  $\bullet\text{NO}_2$  (which yields  $\text{HNO}_2$ ) and  $\bullet\text{OH}$  that yields  $\text{H}_2\text{O}$ .

20 In the following section we undertake the comparison of the energetics of the nitration processes of phenol and 4CP. The elucidation of the 4CP pathway is particularly interesting because it has been found that 4CP photonitration is faster than that of phenol in the aqueous solution.<sup>16</sup>

### 25 Modelling of the reaction between $\bullet\text{NO}_2$ and phenolic compounds

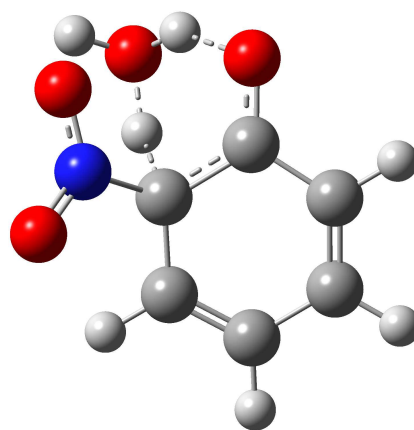
To get further insight into the different reactivity of the studied compounds, a DFT quantum mechanical study was carried out of the ground states of phenol and 4CP. Geometry optimisations and spin distributions of the corresponding phenoxy radicals are reported in ESI. As already mentioned, 4CP only undergoes *ortho* nitration and, to achieve a better comparison between the two substrates, in the case of phenol only the path that yields 2-nitrophenol was considered. An analogous pathway will also yield 4-nitrophenol.

#### Nitration of phenol by $\bullet\text{NO}_2$

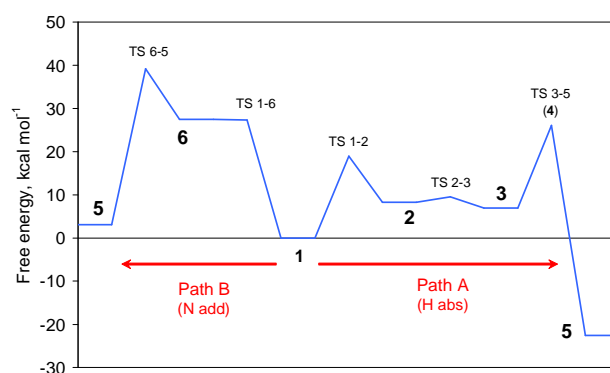
The first mechanism (Path A in Scheme 1) involves first hydrogen abstraction by  $\bullet\text{NO}_2$ , followed by addition of another  $\bullet\text{NO}_2$  to the generated phenoxyl radical **2** to give **3**. A water molecule assists the rearomatisation of the ring to give **5**, through an arrangement of a hydrogen atom in *ortho* to the quinonic oxygen of **3**. In the case of phenol, the transition state **4** for this rearomatization step is depicted in Figure 2.

The other mechanism (Path B, Scheme 1) involves  $\bullet\text{NO}_2$  addition to **1** to give the intermediate radical **6**. In this study we have considered the further reaction of **6** with oxygen, which restores aromaticity upon hydrogen abstraction and yields **5**. Alternative or additional reactants ( $\bullet\text{NO}_2$ ,  $\bullet\text{OH}$ ) could also be involved in the H-abstraction process.

50 Figure 3 shows the free energy profiles of the reactions of  $\bullet\text{NO}_2$  with phenol via Path A and Path B. The calculated energy barriers for the first reaction steps are 19 kcal/mol and 27 kcal/mol for H-abstraction and  $\bullet\text{NO}_2$  addition, respectively.



**Figure 2.** Transition state (TS) **4** for the water-assisted rearomatisation process of intermediate **3** to give product **5**.



**Figure 3.** Free energy diagram for the reaction of phenol with nitrogen dioxide via two possible pathways: hydrogen abstraction (H abs, *i.e.* Path A) and nitrogen dioxide addition (N add, *i.e.* Path B).

By using the well-known Eyring formula<sup>47</sup> within the Transition State Theory (TST) and by comparing the two energy barrier values, one sees a difference of 6 orders of magnitude between the kinetic constants of the two processes, which makes the  $\bullet\text{NO}_2$  addition to the aromatic ring quite unlikely.

Furthermore, the radical intermediate labelled as **6** has very high energy compared to the TS. This increases the probability that  $\bullet\text{NO}_2$  gets away from the ring and goes back to the solution, giving back **1** with a process that has almost no energy barrier. Interestingly, such a conclusion can be reached by considering only the first reaction step, irrespective of the fact that the radical **6** undergoes reaction with  $\text{O}_2$ ,  $\bullet\text{NO}_2$  or  $\bullet\text{OH}$  to finally yield **5**.

In the subsequent steps of Path A, the reaction of **2** with a second  $\bullet\text{NO}_2$  to give **3** is almost barrierless. Indeed, it is a coupling reaction between two radicals and proceeds in solution at a diffusion-controlled rate. The reaction of rearomatisation of **3** through the TS **4** to give **5** has an energy barrier of 19 kcal/mol and is quite exothermic (49 kcal/mol).

These calculated values are in agreement with other values reported in the literature for the ONOO<sup>-</sup>-mediated nitration of tyrosine.<sup>46</sup>

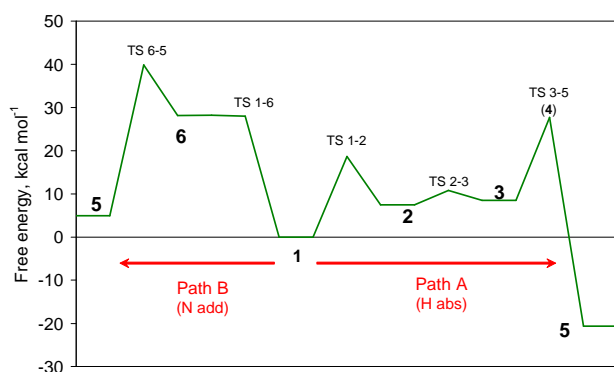
In the case of Path B, after the formation of the intermediate **6**, there is involvement of oxygen in its triplet state that abstracts a hydrogen and re-establishes aromaticity in the ring by forming **5**. This step has an energy barrier of 12 kcal/mol. However, even in the presence of a lower energy barrier that could be afforded by another H-abstrac-

10 reactant, Path B would be considerably more difficult than A. Another interesting issue is that **6** is quite likely to give back **1** because the corresponding process is barrierless. In contrast, in Path A, the back transformation of **2** into **1** would be made more difficult by an energy barrier, thereby enabling the

15 process to also proceed toward **5**.

#### Nitration of 4CP by <sup>•</sup>NO<sub>2</sub>

Figure 4 shows the free energy profiles of the reaction of <sup>•</sup>NO<sub>2</sub> with 4CP via the usual Path A and Path B. The overall profiles are quite similar to those of phenol and, also in this case, it can be clearly seen that Path A (hydrogen abstraction by <sup>•</sup>NO<sub>2</sub>, followed by addition of a second <sup>•</sup>NO<sub>2</sub> to the phenoxy radical) is much favored compared to Path B (addition of <sup>•</sup>NO<sub>2</sub> to the aromatic ring).



**Figure 4.** Free energy diagram for the reaction of 4-chlorophenol (4CP) with nitrogen dioxide via two pathways: hydrogen abstraction (H abs, *i.e.* Path A) and nitrogen dioxide addition (N add, *i.e.* Path B).

#### Comparison of the reaction pathways

The quantum mechanical calculations concerning the nitration of phenol and of 4CP show that Path A, involving an initial H abstraction by <sup>•</sup>NO<sub>2</sub> on the phenolic group to give the phenoxy radical is strongly favoured over Path B, which proceeds via addition of <sup>•</sup>NO<sub>2</sub> to the ring. This computational

35 result is supported by additional experimental evidence, concerning in particular the inability of anisole to undergo photonitration in the presence of either nitrate or nitrite under irradiation, or with their mixture (data not shown). The absence of anisole photonitration can be easily explained in the context of Path A, because the phenolic hydrogen that is

40 involved in the first step of the nitration process is replaced by a methyl group.

By comparing the free energy diagrams relative to Path A

and reported in Figure 3 (phenol) and in Figure 4 (4CP), it can be observed that the difference in terms of energy barriers among the two transition states (TSs) is very low (~0.3 kcal/mol). However, the TS of 4CP is a bit lower in energy than the phenol one, suggesting that the nitration process could be faster with 4CP as substrate, in agreement with the

50 experimental data.<sup>16</sup> This finding could be explained by the inductive effect of the Cl atom, which recalls electron density from the ring and makes the phenolic hydrogen more acidic and, therefore, more liable to be detached (see ESI for details about the spin distribution and for the direct comparison of the two reaction pathways). Indeed, 4CP has a pK<sub>a</sub> value of 9.43, to be compared with pK<sub>a</sub> = 9.99 for phenol.<sup>48,49</sup>

Interestingly, in the case of Path B the energy barrier of the first reaction step (<sup>•</sup>NO<sub>2</sub> addition to the ring) is slightly lower, by 0.7 kcal mol<sup>-1</sup>, for phenol than for 4CP. This probably

60 happens because the inductive effect of the 4CP chlorine atom in the *para* position reduces the ring electron density, thereby inhibiting the ring addition of radicals having an electrophilic character, such as <sup>•</sup>NO<sub>2</sub>. This means that, according to Path B, the nitration of phenol into 2-nitrophenol should be faster than

65 that of 4CP, which is not in agreement with the experimental results.<sup>16</sup>

The fact that Path A predicts the correct reactivity order of phenol and 4CP toward nitration, differently from Path B, constitutes additional evidence that the photonitration of both

70 compounds involves H abstraction by <sup>•</sup>NO<sub>2</sub> as the first reaction step.

It is also possible to derive within the TST the microkinetic constants of H-abstraction from the values of the energy barriers.<sup>47</sup> The calculated rate constant ratio k<sub>4CP</sub>/k<sub>phenol</sub> is 1.7.

75 By assuming, as derived in the present paper, that <sup>•</sup>NO<sub>2</sub> is involved in the photonitration of both phenol and 4CP, the experimental data give a ratio of 5.8.<sup>16</sup> The fact that theoretical calculations are able to correctly predict at least the order of magnitude of the ratio is a good result, but it

80 should be reminded that it is very risky to make reasonable scientific speculations on such small energy differences (< 2 kcal/mol) as have been observed between the TSs of phenol and of 4CP. Indeed, it is not possible to ignore the errors caused by both the basis set/functional used and the TST,

85 which would not be very far from the energy differences involved.<sup>50</sup>

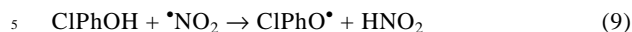
Note that path A predicts the formation of HNO<sub>2</sub> in its first step, and HNO<sub>2</sub> could be easily oxidised to NO<sub>3</sub><sup>-</sup> + H<sup>+</sup> under the adopted photochemical conditions. However, path B

90 yields HO<sub>2</sub><sup>•</sup> (pK<sub>a</sub> = 4.8<sup>51</sup>) that would be readily deprotonated to O<sub>2</sub><sup>-•</sup> + H<sup>+</sup> at the adopted initial pH of 6. Therefore, path A and path B would cause a comparable acidification. More importantly, acidification from the cited processes would be largely overcome by the consumption of H<sup>+</sup> upon photolysis

95 of nitrate and nitrite (reactions 1,2). These issues prevent the experimental demonstration of the occurrence of path A by direct pH measurements.

## Comparison with the experimental data

A 4CP nitration mechanism that follows Path A would involve the following reactions, where CIPhOH is 4CP and CIPhO• is the corresponding phenoxy radical:



The lumped reactions (11,12) include several transformation pathways of CIPhO• and •NO<sub>2</sub>, among which are the reactions with superoxide.<sup>18,45</sup> The formation of •NO<sub>2</sub> takes place via reactions (1) and (3) and, because  $R_{\text{OH}}^{\text{NO}_3^-} = R_{\text{NO}_2}^{\text{NO}_3^-}$ , it is  $R_{\text{NO}_2} = R_{\text{OH}}^{\text{NO}_3^-} + k_3 [\bullet\text{OH}] [\text{NO}_2^-]$ , with  $[\bullet\text{OH}] = R_{\text{OH}} (k_4 [4\text{CP}] + k_3 [\text{NO}_2^-])^{-1}$ . Upon application of the steady-state approximation to CIPhO• and to •NO<sub>2</sub> one gets the following expression for the NCP formation rate:

$$\frac{d[\text{NCP}]}{dt} = \left( R_{\text{OH}}^{\text{NO}_3^-} + R_{\text{OH}} \cdot \frac{k_3 [\text{NO}_2^-]}{k_3 [\text{NO}_2^-] + k_4 [4\text{CP}]} \right) \cdot \frac{k_9 [4\text{CP}]}{k_9 [4\text{CP}] + k_{12}} \cdot \beta \quad (13)$$

where  $\beta = k_{10} [\bullet\text{NO}_2] (k_{10} [\bullet\text{NO}_2] + k_{11})^{-1}$  is the fraction of CIPhO• that reacts with •NO<sub>2</sub> to yield the 4CP. With the known values of  $R_{\text{OH}}^{\text{NO}_3^-}$ ,  $R_{\text{OH}}$ ,  $k_3$  and  $k_4$  it is possible to fit the experimental data of NCP formation rate with equation (13), obtaining  $\beta = 0.082$  and  $k_{12} k_9^{-1} = 7.7 \cdot 10^{-5} \text{ M}$ . The fit is shown as the dashed curve in Figure 1 and it is in good agreement with the experimental data ( $R^2 = 0.97$ ).

## Conclusions

The experimental data reported in this paper allow exclusion of a 4CP nitration process that takes place via •OH + •NO<sub>2</sub>. The same process could be excluded for the photonitration of phenol.<sup>40</sup> In contrast, nitration of both phenolic compounds should involve •NO<sub>2</sub> alone. The are two possible pathways that could account for the nitration of phenol and of 4CP by •NO<sub>2</sub>. Path A proceeds via H abstraction by •NO<sub>2</sub> on the phenolic oxygen to give HNO<sub>2</sub> and the corresponding phenoxy radical. The latter reacts with another •NO<sub>2</sub> to finally yield the nitrophenol. Path B involves addition of •NO<sub>2</sub> to the aromatic ring, followed by H abstraction operated by O<sub>2</sub>, •NO<sub>2</sub> or •OH to give the nitrophenol. Quantum mechanical calculations, carried out following the DFT theory indicate that path A would be strongly favoured over B because of the much lower activation energy barrier. Moreover, the energetics of path B suggests that the reaction intermediate would be decomposed back to the reactants far more easily than it can evolve into the nitrophenol product. Finally, path A correctly predicts that the nitration of 4CP is faster than that of phenol,<sup>16</sup> because the chlorine substituent on the ring makes the phenolic hydrogen more acidic and favours the formation of the phenoxy radical. An additional issue is the lack of anisole nitration in the presence of nitrate and/or nitrite under irradiation. It is consistent with the occurrence of path A, because in anisole the phenolic hydrogen is replaced by a methyl group. Nitration of 4CP via Path A also allows

the elaboration of a kinetic model that is in good agreement with the experimental data.

Nitration of phenolic compounds would thus involve two •NO<sub>2</sub> radicals, which has implications for the use of phenol as a probe molecule for nitrogen dioxide. Indeed, phenol photonitration can be adopted to derive the formation rate of nitrogen dioxide in an irradiated sample. The •NO<sub>2</sub> formation rate calculated under the hypothesis that two •NO<sub>2</sub> are involved in nitration is exactly the double than for the case where nitration involves just one •NO<sub>2</sub>. Therefore, the involvement of two •NO<sub>2</sub> in phenol photonitration via Path A should be taken into account when using such a reaction as a •NO<sub>2</sub> probe in solution.

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## Notes and references

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